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SOME ASPECTS OF EVOLUTION[1]

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IN his much-discussed presidential address at the 1914 meeting of the British Association, the great skeptic William Bateson finished with the following sentence: "Somewhat reluctantly and rather from a sense of duty I have devoted most of this address to the evolutionary aspects of genetic research. We can not keep these things out of our heads, as sometimes we wish we could. The outcome, as you will have seen, is negative, destroying much that till lately passed for gospel." This negative standpoint was certainly justified to a certain extent by the results of early Mendelian work, which led more in the direction of evolutionary skepticism than optimism. Almost twenty years have passed since, which have witnessed an unbelievable increase in the knowledge of genetical facts. And whereas, as Bateson says, we can not keep these things, namely, the evolutionary aspect of genetics, out of our heads, geneticists from time to time like to leave their bottles, breeding cages and seed pans and to review the advances of experimental work in regard to their bearing on problems of evolution. I must confess to have been repeatedly guilty myself of this sin during the past 15 years, with the result that the curve of my deliberations was oscillating between skepticism and optimism and still is doing so. Let me not be misunderstood: not skepticism in regard to evolution, which I regard as a historic fact, as all biologists do; but skepticism and optimism regarding the insight into the means of evolution on the basis of genetic facts.

You all know that the majority of the geneticists are to-day rather optimistic. Genetic experimentation certainly has shown that the sudden changes of the hereditary units, the genes, called mutations occur with sufficient frequency to furnish material for selection; it has shown that in plants at least considerable changes, amounting to the formation of

[1] Paper read at a general meeting of the American Association for the Advancement of Science, in Chicago, June, 1933.

what might be termed new species, may be brought about by the different types of chromosome-arrangements which play such an important rôle in present genetical research; and genetics may rightfully claim to have performed experimental changes of forms into other different ones by means which could be conceived as effectual occasionally also in nature; this is at least true for the plant kingdom, but not for animals. In addition, it has been shown that after all Darwin's theory of selection, if properly applied and based upon the present-day knowledge of what Darwin termed generally variation, is still the best guide to an understanding of some of the ways of evolution. This means that, given a certain frequency of mutations, which produce slight changes in a haphazard way and given the selective action of the environment which wipes out certain mutations and lets pass or even favors others, considerable transformations are possible within the time available for evolution. It is not my intention to enlarge here on this topic, which has been treated repeatedly in recent years by leading geneticists. But I have not been satisfied yet that these groups of facts and conclusions, important as they are, tell us the whole story; and I believe that, especially for the animal kingdom, much work has still to be done before we can see clearly how evolution, which we can observe in its great lines as an actual historic fact, has proceeded in detail. I should like then to discuss a few of the fundamental questions regarding the first steps of evolution in nature, which I met in the course of my own experimental work, and then bring to your attention some facts and lines of thought which might assist a deeper insight into our problem.

When Darwin spoke of the origin of species, the Linnean species seemed to be a rather clear-cut unit. Meanwhile we have recognized the existence of micro-species and of subspecies and racial groups, and if we were to define the units which are meant if we are talking about the origin of species, the difficulties would be found insurmountable. In one taxonomic group, what is called a species is hardly distinguishable from the next species, and in another taxonomic group, the species are more different than genera in the first. In my younger days I was working on the minute histology of the nematode worms *Ascaris lumbricoides* and *megalocephala*. These species, though well known to every zoologist as very much alike, proved to be different practically in every cell of their body. At that time I could have undertaken to determine the species from a single isolated cell of many organs of these worms. Compare with this the almost complete impossibility of distinguishing a lion's and tiger's skeleton, in order to realize the hopeless situation for a proper definition. As a matter of fact the only case of a taxonomic difference between two forms, which can be properly defined, is the difference between a homozygous strain of an animal or plant and one of its mutations. Then, if we are talking about the formation of species, what we actually mean is the origin of very different forms within a group, without consideration of their taxonomic designation as species, genera or even families, which more or less depends upon the personal judgment of the taxonomist.

The majority of the geneticist's work is done with domestic animals and plants or with such wild forms as have given plenty of mutations under cultivation. The obvious reason is that natural species or still more distant units are either sterile *inter se* or produce sterile hybrids and therefore do not lend themselves to the methods of genetic analysis by hybridization.

There is only one taxonomic category about which genetic research has given us proper information: This is the so-called Rassenkreis, a conception which in some taxonomic groups, as birds and mollusks, is gradually replacing the species concept. A Rassenkreis is a series of typically different forms or subspecies found at different points within the geographic range of a species and often showing a typical order of their characters if arranged geographically. As the end members of such a group might be rather different, the idea has arisen that the formation of a geographic Rassenkreis is the beginning of speciation. The idea is that distant members of such a group become finally isolated and will come under the influence of new selective agencies, which carry the stream of further mutational changes into new directions towards the formation of new species and genera. Further, whereas it is found that the differential characters of these subspecies may have adaptational value, it is frequently reasoned that the influence of the environment has produced these forms. To quote only one prominent witness: Henry Fairfield Osborn in a recent address has stood up most emphatically in favor of such views. He writes:

> . . . the Buffon-St. Hilaire principle of direct environmental action both on body and germ is now universally admitted as one of the great causes of evolution. As shown in the experiments of Sumner it is directly responsible for speciation in animals like Peromyscus (a deer mouse). Sumner has positively demonstrated that modifications in color and form and proportion traceable to the prolonged direct action of environment, are hereditary and therefore true germinal characters. Perhaps the best established zoological generalization of modern times is that subspeciation, and ultimately full speciation is the inevitable result of prolonged change of environment. . . .

I am sorry to say that I can not agree with the eminent paleontologist, either in regard to the evolutionary nature of subspecies or in regard to the origin of their adaptational traits. Simultaneously, with Sumner's work on Peromyscus I have analyzed the case of the geographic variation of the gipsy-moth *Lymantria dispar,* and owing to the great regularity of behavior of these geographic races in respect to climatic conditions and also to the possibility of working with large numbers, I was able to make what I believe to be the most complete genetic analysis of a Rassenkreis. As a matter of fact, where Sumner's and my work is comparable the results are also identical, as far as facts are concerned. And I would do injustice to Sumner if I would not state that in his last review of his work he expresses himself rather cautiously in regard to the conclusions to which Osborn points, saying, "While admitting the paucity if not the total lack of direct evidence in this field I still lean strongly towards the view that the process of natural selection must be supplemented by adaptive responses of a more direct nature."

My own work, however, permits, I think, of taking a definite stand towards both problems, mentioned in Osborn's sentence which I quoted before, namely, the problem whether the formation of subspecies is the beginning of speciation and whether unknown actions of the environment are responsible for the adaptational features of geographic variation. Regarding the second point, I could prove that certain characters of a more physiological order show within the geographic range of the species a gradient of different heritable conditions which are perfectly parallel to a gradient of certain climatic conditions. For two of these characters, namely, the length of time of hibernation, the so-called diapause and the rate of larval growth, it could be shown in detail that the definite hereditary type found in definite areas constitutes an adaptation of the life-cycle of the animal to the seasonal cycle of nature. To mention only one example, which is typical for all similar cases: In a region with strong winter and short summer the hibernating individuals would be wiped out if they hatched too early; on the other side, the race would be wiped out if they hatched so late that the short summer would not give them enough time to finish their life-cycle. Correspondingly, the genetic constitution of the races inhabiting such a region is such that a certain sum of heat makes the individual hatch within a short time, whereas races inhabiting warmer areas with mild winter require a much larger sum of heat for the same purpose, also on a hereditary basis. And of course all imaginable intermediate conditions are also found in their proper area.

Here, then, we have a series of typical adaptations to the conditions of a series of typically different environments, and these adaptations are caused by different constitutions in regard to Mendelian genes. Changes in the genetic make-up concerning individual genes are known thus far only to occur in the form of mutations, and no geneticist will doubt therefore that also in this case the different genetic constitutions of the races, those with and those without adaptational value, are the result of mutations and their proper recombinations which once must have taken place in the same manner as mutations observed in the laboratory. But how about the adaptational side, in our case the close parallel between the gene-controlled details of the life-cycle which we just mentioned and those of the seasonal cycle in different regions? If I am not mistaken, Davenport and Cuénot were the first to pronounce the principle of preadaptation, which to most, if not all geneticists, seems to furnish the only workable idea in cases like the one here discussed. Preadaptation means that adaptations are not originated in the surroundings in which they are found and also not caused by whatever action of these surroundings; moreover, adaptive characters appear as chance mutations, without any relation to their future adaptational value, as preadaptations. But these changes allow the organism to migrate into new surroundings, into which it will fit on the basis of its preadaptations. Applied to our case, it would mean that among the population in the original environment mutations were found which produced different conditions in regard to adaptational characters, in our example, mutations which prolong or shorten the inherited length of the hibernation period. Such mutated forms were preadapted to another environment. Brought by chance into another environment with a correspondingly different seasonal cycle, they were able to establish themselves. It is needless to say, then, that we must regard such preadaptational mutations as a prerequisite for the spreading of a species into new areas with different conditions, which would be inaccessible to the original form, and therefore also for the formation of geographic races or subspecies; and further that it will be the physiological characters, not the visible traits, which will be of primary importance in this case. In my material, Lymantria, as a matter of fact the diversity of physiological characters is considerably greater within the Rassenkreis than the diversity of forms which the taxonomist could recognize.

May I mention finally two facts which show the principle at work in our material. Every American knows that the few caterpillars of the gipsy-moth which were blown out of Monsieur Trouvelot's window two generations ago established themselves only two

well in Massachusetts. In the light of our work their hereditary life-cycle must have been well preadapted to the seasonal cycle in Massachusetts. The same moth has been introduced into England any number of times, but never was established, in my opinion only for lack of preadaptation to the seasonal cycle. The second fact is the following: Some years ago, I had succeeded in producing mutations in Drosophila by the action of high temperature. The Japanese geneticist, Y. Tanaka, informed me then that he succeeded in producing mutations in the silkworm by a similar method applied at a definite stage. I then occasionally treated the gipsy-moth in a similar fashion. One mutation, which was produced, made the young caterpillars hatch without hibernation. Within the present range of distribution of the moth, such a mutation, if occurring in nature, would be absolutely lethal, because in a moderate climate there would be no possibility of finishing a second generation before winter sets in. But introduced into a tropical climate, the same mutation might permit the otherwise unlikely establishment of the form. I do not doubt, then, that the adaptational side of the facts of geographic variation is to be explained on ordinary genetic grounds, namely, chance mutation of preadaptational nature within a population and subsequent migration into and survival in another suitable area. I may add finally that our material is not the only example, but that Brown has since found a parallel case in Daphnids and that also Turesson's work on ecospecies in plants fits perfectly into these lines.

Let us turn now to the other problem stated above and answered in the affirmative by Osborn and probably by most taxonomists: Is the formation of geographic subspecies the beginning of speciation? My own work was started with the idea of proving that it was. As I have already stated at last year's International Congress of Genetics, the results of the analysis led me to the conclusion that it was not. The different subspecies in the different regions occupied by the species are genetically different in many characters. Most of these are found to form quantitative gradients which run parallel to definite features of the climatic conditions. But the series of local changes in regard to one character is not exactly paralleled by those of other characters, so that in a given area one hereditary and differential character might be found over the whole area, another be subdivided into three types and another into more types. But I was unable to find one or a combination of subspecific characters which could be regarded as leading out of the limits of the species or towards another one.

There are found within the same region two other species of the same genus which show practically the same life-cycle and which must be adapted to the same general features of the region. But they are different in practically every detail of their form, structure, larva and even their type of genetic variation. Of course their differences might be also adaptational in a certain sense. But here is the great difference: The different adaptational characters of the subspecies are of a quantitative nature, and show a plus-minus character. For example, we find a longer diapause in warmer and a shorter in colder regions, similarly different rates of development, different sizes, degrees of pigmentation, etc. The adaptation to local conditions then takes place by genetic shifts of a quantitative nature within the typical characters of the species and, as I may now add, running in the same directions as the non-heritable reactions to the environment. The different species, however, may solve one and the same adaptational problem by entirely different methods. For example, the species *Lymantria dispar,* the gipsy-moth, lays her eggs in the shade on wooden or stony surfaces and covers them with a sponge-like mass of hair, the problem being to ensure proper conditions for hibernation, especially regarding moisture. The nearly related species, *L. monacha,* pastes her eggs without covering into clefts of the bark of trees, and another species, *L. mathura,* still in the same area, lays below the bark and within a cement-like mass. Of course, within the different genetic systems represented by related species, parallel types of genetic variation, subspeciation, may be found, as is well known. For example, many species of rodents may form pale desert forms, and many species of birds form subspecies with brighter colors in warmer climates. But in other cases even the trend of genetic variation might be different: *Lymantria monacha* tends towards formation of melanic forms; *L. dispar* does not. These two species are able to spread all over the moderate regions by proper adaptive changes, but not into the tropics, the nearly related species *L. mathura,* however, inhabiting certain regions together with the former, spreads into the tropics but not into cold regions.

I am perfectly aware of the dangers of generalizing from one case, even the best known one. I know also the objections to such conclusions, for example: There are Rassenkreise, the most distant members of which might be so different that in case of isolation they might become the starting point for quite new developments towards another species. Looking closely at the facts concerning the typical differences within a Rassenkreis, I can not see why the isolation of two members of a Rassenkreis could give better chances for new developments than the isolation of individuals within a subspecies: The changes necessary for the formation of a new species are so large that the relatively small differences of the subspecies as a starting point would hardly count. And I can not help

confessing that after trying to get acquainted with the taxonomist's material, the skeptical standpoint derived from my own genetic analysis could not be shaken. There is in my opinion no reliable fact known which would force us to assume that geographic variation or formation of subspecies has anything to do with speciation; the results of genetical analysis and of sober evaluation of the other facts are positively in contradiction to such an assumption.

We just mentioned the fact that different species—and also as a matter of fact members of different families—may show a trend towards formation of comparable mutations and parallel series of subspecies, which are, after all, combinations of mutations strained through the sieve of fitness to environment. It is known that especially Vavilov has made such facts the basis of evolutionary considerations. But we also mentioned that nearly related species might show different trends of genetic variation. And this leads us to a point which, I believe, will be considered of paramount importance in future discussions of evolution. The transformation of one species into another is possible only if permanent changes in the genetic make-up occur, and if the changed forms stand the test of selection. Both these points have long been in the foreground of evolutionary discussion. But there is a third point, often neglected, which lies, I think, at the basis of the whole problem, namely, the nature of the developmental system of the organism which is to undergo evolutionary change. The appearance of a genetic form, whether we call it a species or a genus, which is to be considerably different from the ancestral forms, requires that a considerable number of developmental processes between egg and adult have to be changed, in order to lead to a different organization. Development, however, within a species is, we know, considerably one-tracked. The individual developmental processes are so carefully interwoven and arranged so orderly in time and space that the typical result is only possible if the whole process of development is in any single case set in motion and carried out upon the same material basis, the same substratum and under the same control by the germ plasm or the genes. From this it follows that changes in this developmental system leading to new stable forms are only possible as far as they do not destroy or interfere with the orderly progress of developmental processes. Of course, everybody knows that this is the reason why most mutations are lethal. But not everybody keeps in mind that here also is touched one of the basic points of the problem of evolution. The nature and the working of the developmental processes of the individual then should, if known, permit us to form certain notions regarding the possibilities of evolutionary changes.

There are, as far as I can see, two general notions in regard to the causal understanding of individual development which are of importance for the problem under discussion. One is the notion which I have tried to develop from experimental evidence that the action of the genes in controlling development is to be understood as working through the control of reactions of definite velocities, properly in tune with each other and thus guaranteeing the same event always to occur at the same time and at the same place, as worked out in detail in my physiological theory of heredity. The second notion is that derived from the results of experimental embryology. It says that two types of differentiation are closely interwoven in the process of development, namely, independent and dependent differentiation. Independent differentiation means that a once started process of differentiation takes place within an organ or part of the embryo, even if completely isolated from the rest; dependent differentiation, however, requires the presence and influence of other parts of the embryo for orderly differentiation. If, for example, the group of cells which is to be regarded as the primordium of an eye in the embryo of a vertebrate, is removed from its proper place, it will nevertheless be able to develop into an eye. If, however, the part of the skin of the head which is to form the lens of the eye is isolated, no lens is formed because the presence of the eye is necessary for the determination of a lens. Such are the two general notions, which together describe fairly well the essentials of gene-controlled development, namely, the notion which considers development as an orderly interwoven series of developmental reactions of definite velocities, properly in tune with each other, and the notion of dependent and independent differentiation. Both together will allow us to discuss some of the possibilities of evolutionary change as viewed from the standpoint of stable, orderly development.

Let us begin with an experimental fact. It has been known for a long time that it is possible to change the appearance of certain butterflies by proper experimental procedure within a sensitive period of development so that they can not be distinguished from heritable geographic subspecies found in nature in other regions. If, for example, the young pupa of the Central-European swallowtail is treated with extreme temperatures, some individuals will hatch which can not be distinguished from the typical forms inhabiting Palestine. Of course the characteristic features are not heritable in the former case, but strictly heritable in the latter. These and similar facts have since been extended in many ways, also to cases of ordinary gene mutations. I was, for example, able to produce in similar experi-

ments with Drosophila the non-heritable likeness of many well-known mutations. I do not doubt either that it would be possible to perform the same experiment in regard to any known mutations, if the proper method would be found. Speaking generally, this would mean that the more frequently occurring genetic changes, called mutations, are such as change certain developmental processes in a direction which lies within the ordinary range of changes which might occur within the developmental system under purely environmental influences. An explanation is very simple on the basis of the assumption that in the developmental processes in question reaction-velocities are involved; the external influences in question change the rate of some reaction or system of reactions underlying the differentiation of the character in question and the mutation which produces the same phenotypic effect is a change in a gene, which controls the same differentiating reaction, with the effect of a corresponding change of the speed of the reaction. It is perfectly clear, then, that within similar developmental systems, represented by taxonomically related forms, the same types of mutational changes, parallel mutations, will have the greater chance of not being lethal, because in such a system of exactly tuned and interwoven reactions, only few changes of the rate of individual processes will be possible which do not interfere with the others. And there is another consequence: if there are only a few avenues free for the action of mutational changes without knocking out of order the whole properly balanced system of reactions, the probability is exceedingly high that repeated mutations will go in the same direction, will be orthogenetic. Orthogenesis means that evolution, once started, proceeds further in exactly the same direction until sometimes extreme forms are evolved which lead to the ultimate extinction of the whole line. Paleontologists have found the most beautiful examples of this type, facts with which any theory of evolution has to reckon. Many theories have been advocated to explain such facts. We have pointed out a long time ago and still hold that orthogenesis is not the result of the action of selection or of a mystical trend, but a necessary consequence of the way in which the genes control orderly development—a way which makes only a few directions available to mutational changes, directions which if once started and not acted upon by counterselection, will be continued. I shall not go into the purely genetic details of such a situation. But it might be mentioned that recently some of the younger generation of paleontologists (Beurlen, Schindewolf, Kaufmann) have taken up these views. This is indeed very gratifying, because the problem of orthogenesis has always been a stumbling block to an understanding between geneticists and paleontologists.

At this point, we have to think of the second notion, mentioned before, regarding the general control of embryonic differentiation, namely, dependent and independent differentiation. It is obvious that processes of dependent development are so closely linked with the whole of normal development that mutational changes within them can hardly lead to a normal organism. It is therefore to be expected that successful mutations of eventual evolutionary value act upon such developmental processes which themselves are not inductive of further important steps. This means that viable mutations will mostly be concerned in the animal kingdom with end-processes of embryonic differentiation, affecting the organism only after the characteristics of the species have been laid down.

But how about the possibility of occasional successful mutational changes acting upon earlier developmental processes? Would such a change, if possible at all without breaking up the whole system of the orderly sequence of development, not at once have the consequence of changing the whole organization and bridging with one step the gap between taxonomically widely different forms? Let us for a moment dwell upon such an idea, which I pointed out a long time ago as a logical consequence of my views on gene-controlled development and which has repeatedly cropped up since in evolutionary literature (*e.g.*, De Beer, Haldane, Huxley). Again, the most probable mutational change with a chance to lead to a normal organism is a change in the typical rate of certain developmental processes. Of course, in most cases such a shift of a partial process would lead to the production of monstrosities and, as a matter of fact, Stockard has always advocated such a cause for many monstrosities. But we must not forget that what appears to-day as a monster will be to-morrow the origin of a line of special adaptations. The dachshund and the bulldog are monsters. But the first reptiles with rudimentary legs or fish species with bulldog-heads were also monsters. Correspondingly, we certainly know of many cases of mutational shifts of the rate of certain developmental processes leading to non-viable results, for example, caterpillars with pupal antennae, larvae of beetles with wings and similar cases of so-called pro- and opisthotely. But I can not see any objection to the belief that occasionally, though extremely rarely, such a mutation may act on one of the few open avenues of differentiation and actually start a new evolutionary line. Let us assume a mutational change in rate of differentiation of the limb-bud of a vertebrate, to take up the example just mentioned. The consequent rudimentation of the organ would probably not interfere with orderly development of the organism. Here, then, an avenue would be open to considerable

evolutionary change with a single basic step, provided that the new form could stand the test of selection, and that a proper environmental niche could be found to which the newly formed monstrosity would be preadapted and where, once occupied, other mutations might improve the new type. And in addition, the possibility for an orthogenetic line of limb-rudimentation would be a further consequence in accordance with what we have heard before. Of course, these are speculations, which we can not help but enjoy occasionally as long as unfortunately there is no way visible of attacking such problems with the methods of genetics. But meanwhile some important insight might already be gathered from purely morphological work, as that of Sewertzoff, or experimental work of the type of Twitty's work on rudimentary eyes.

At the best, such viable mutations concerning rates of earlier developmental processes must be rare, even when processes are involved such as the differentiation of appendages which are not so closely interwoven with the whole of development. Still lower is the chance if we try to imagine changes in differentiation which are of consequence for the whole of development. Let our imagination run wild for a moment and let us consider the possible event of three more and more violent and therefore less and less probable changes of the type under consideration, produced by a viable mutation acting upon earlier embryonic differentiation by changing relative rates of development. D'Arcy Thompson has shown that extremely different forms of organs or of whole organisms may be geometrically transformed into each other by a Cartesian transformation of the system of coordinates. Translated into phylogenetic language, this would mean that immense evolutionary effects could be brought about by changing the differential growth rates of the whole body or organ at an early point in development, with all the necessary secondary effects of such a change. I could imagine, and I have actually pointed out, that a single mutation involving the rate of one of the important reactions connected with growth, acting on the principle underlying Thompson's transformations, could start a perfectly new evolutionary line, leading at once far away from the original form and being able to be completed by orthogenetic development within the once blasted new avenue. Or another example: There are innumerable cases known where no intermediate forms between two extremely different ones are imaginable. Take, for example, the Pleuronectid fishes, the flounders and their kin, lying flat on one side, the eyes being translocated during embryonic development to the other side with all the following asymmetries of skull, fins, muscles. Cuénot expressed his conviction a long time ago that no slow accumulation of variations and selections is needed to explain the origin of such forms. There exist flat symmetrical fishes with the habit of resting lying flat on one side. Given the proper arrangement of the eye muscles and the interorbital septum of the skull, a single step was only necessary to start the migration of the eye, all the rest of the transformations being necessary consequences of the first step. I can not help agreeing with Cuénot and adding that at the proper moment in the evolutionary line a single mutation in regard to the rate of certain embryological processes of the type which ordinarily produce a monster, may have given birth to a monstrous new family with all its essential traits and preadapted to certain modes of living. Of course the further differentiation, the slow evolutionary working out of the details, would be brought about by new mutations of the different types, including as well other large steps, as accumulations of small mutations under the influence of selection.

A third example, which I have repeatedly used to explain the general idea, appears still more fantastic. Let us consider one of the famous lines of transformation which the comparative anatomy of vertebrates has brought to light, for example, the series of transformations of the visceral arches. I believe that these facts constitute one of the most beautiful proofs of evolution; and in addition I believe that their analysis by the methods of comparative anatomy is one of the greatest achievements of biological thinking, though some biologists of to-day are inclined to prefer the most meaningless experiment to such a piece of masterful morphological analysis. In the case of the visceral skeleton we see, for example, that the so-called hyomandibular bone of fishes loses its function as connective element between jaws and skull, and is transformed into an auditory ossicle situated within the skull and playing an important rôle in the transmission of sound, a transformation which takes place simultaneously with the appearance of the tympanical membrane as adaptation to terrestrial life. In this transformation two major steps are observed: First, the formation of a new connection between skull and jaw, thus excluding the hyomandibular bone from its former function; second, the appearance of the tympanical membrane in this region and the inclusion of the hyomandibular bone into the ear cavity, with the change of its function to that of an auditory ossicle. The first step is found in the Crossopterygian fishes, the second in Amphibia. In both cases a slow transformation by accumulation of advantageous mutations is hardly imaginable. There are no steps possible between a tympanical membrane and none and also no steps between two

types of articulation of the jaw with the skull. But I could not find much difficulty in the idea that the decisive step was taken by a single mutation affecting the relative rate of differentiation of the cranial end of the hyoid arch from which springs the hyomandibular bone, with the effect of forcing these parts, left behind in development, into new surroundings and connections, where future developments could make use of them for quite different purposes. It would certainly be of no use, and sheer speculation, to try to work out such an idea in detail. But I think that we can get hardly around the principle underlying it. Of course, there is no way visible to attack such a problem by the methods of genetical research. But I am not so sure that this means that it can not be attacked at all.

At the beginning of this lecture I said that my mind, like that of many geneticists, is oscillating between skepticism and optimism with regard to the views on the means of evolution as derived from genetical work. I have now presented to you examples of both states of mind: First, a bit of skepticism with regard to the rôle which the formation of geographic races or subspecies may have played in evolution; and then a bit of optimism in trying to show that the physiological system underlying orderly development, on the basis of the genetic constitution, allows some of the larger steps in evolution to be understood as sudden changes by single mutations concerning the rate of certain embryological processes. But whoever tries to formulate views on the means of evolution on the basis of the actual knowledge of facts must be aware that any day new facts might come to light which could force our ideas into quite different channels. Therefore I wish to return at the end of this lecture again to the results of actual experimentation and to draw your attention to some new lines of experiment which perhaps will finally influence our general conceptions considerably.

A number of years ago I found, as already mentioned, that it is possible to produce gene mutations by the action of extreme temperatures of almost lethal dose. Unfortunately, there is still an unknown element in the technique of these experiments which makes success dependent upon some conditions which have not been isolated as yet. Progress in this line of research is therefore slow. One of the most startling results of this work was that in a series of experiments a few mutations were always produced again. Jollos, who continued this work, had similar results, but in his experiments other mutations were preponderant and also appeared over again. I then repeated the experiments and in successful cultures had now the same mutations which appeared also in Jollos' cultures. Thus it seems that there is a relation between stimulus, maybe also material, and the type of genetic response. There was another interesting result. I have mentioned already that in such experiments quite a number of phenotypic changes are produced which resemble well-known mutations, but are of the nature of non-heritable modifications. In a few instances, cases were found where the treated animals themselves showed such a visible change, namely, dark body color, and where the offspring of the same animals showed the same phenotype as mutation. The explanation which had to be given to such a case of so-called parallel induction was that there was simply a chance-overlapping of two independent phenomena, namely, the production of a modification and of a mutation of the same phenotype; this would be made possible by the aforementioned assumption that in both cases the same developmental process was changed either by environmental action or by genic action.

But there were still other strange facts. I had observed that the typical non-heritable changes which resembled heritable mutations in appearance, and which always were found in the flies which had been treated with heat during definite larval stages, were different, if the details of treatment were changed. For example, with one type of treatment, a certain peculiarity of the wing-shape was produced; with another type of treatment the majority of changed individuals presented a very different type of wingform. In recent experiments, Jollos, who had had the same experience, could add some most interesting facts. In the lines with ordinary treatment the most frequent mutations were those of body color, called sooty, and of eye color, called eosin. If the usual treatment was replaced by one with dry heat, the non-heritable variations which appeared in the treated animals were of a different type than usual. Predominant were flies with extended wings, with curly wings, with asymmetrically shortened wings and with scalpelliform wings. Jollos continued treating the normal offspring of these lines with the same method, and during the following generations a number of mutations appeared, some repeatedly; and among these were the mutations, the phenotype of which is identical with the forementioned non-heritable variations produced in the same line, namely, extended, curly, scalpelloid and asymmetrically shortened wings. Of course, this has nothing to do with an inheritance of acquired characters; the mutations had appeared among the offspring of normal individuals. There are now altogether seven cases in which a mutation has been produced in the same lines in which exactly the same phenotype occurs frequently as a nonheritable modification as a consequence of the same

treatment. Among these seven cases, one of which was found by myself and the others by Jollos, is one mutation which before was observed only once in the whole Drosophila work and two which had never been observed.

These certainly are interesting facts, which might lead to strange consequences. I personally am willing to wait for further results before drawing conclusions. Jollos, who has not yet published the results which I quoted, permits me to mention that he is inclined to derive the following interpretation: The genes produce within the protoplasm active stuffs which are of the same constitution as the genes themselves. Both will react in the same way upon external conditions, but those within the protoplasm easier than those protected within the chromosomes. Such a view, of course, would lead to many interesting consequences. We shall, however, dismiss the subject with the mention of the actual facts, which one day may be of great importance not only for problems of special genetics but also for discussions on evolution.

The title of this lecture was: "Some Aspects of Evolution." But as I said at the beginning, it was not meant that the idea of evolution itself, which all biologists consider a historic fact, should be under discussion, but some of the ways and means by which nature makes the transformation of species possible. The three aspects which I chose for representation were, first, an aspect where I had to express skepticism in regard to well-established beliefs. I tried to show on the basis of large experimental evidence that the formation of subspecies or geographic races is not a step towards the formation of species but only a method to allow the spreading of a species to different environments by forming preadaptational mutations and combinations of such, which, however, always remain within the confines of the species. The second aspect which I discussed was one where I felt again optimistic. I tried to emphasize the importance of the methods of normal embryonic development for an understanding of possible evolutionary changes. I tried to show that a directed orthogenetic evolution is a necessary consequence of the embryonic system which allows only certain avenues for transformation. I further emphasized the importance of rare but extremely consequential mutations affecting rates of decisive embryonic processes which might give rise to what one might term hopeful monsters, monsters which would start a new evolutionary line if fitting into some empty environmental niche. Finally, I discussed a third aspect of the problem, this time under the slogan of watchful waiting, namely, new lines of genetic research concerning the problem of mutation and therefore also of evolution. With these discussions we touched certainly only a small fraction of the manifold problems of evolution. But if we would try to visualize all the contributions which the science of genetics has recently made in this direction, we might be entitled to say that our insight into one of the most complex biological problems is constantly increasing. Progress of science follows of course a slowly ascending, wavy curve, with always recurring valleys. But viewed from some distance, the waves disappear and only the upward trend remains visible. Such is also the case with our knowledge of the methods and means of evolution.

OBITUARY

MEMORIALS

CEREMONIES commemorating the one hundredth anniversary of the birth of Dr. Carlos J. Finlay, who first advanced the theory that mosquitoes were carriers of yellow fever, were held at the Cuban Embassy on December 3. The ceremonies were due to the initiative of the Washington chapter of the Pan-American Medical Society, with Dr. Manuel Marquez Sterling, diplomatic envoy of the Cuban Government, acting as host. The program included addresses by Dr. Sterling, Senor Don Luis M. de Iruju, Spanish chargé d'affaires; Colonel Roger Brooke, of the Army Medical Department; Dr. L. O. Howard, Brigadier General J. R. Kean and Dr. Victor Alfaro.

MRS. ERNEST HOWE, of Litchfield, Conn., widow of Ernest Howe, who died last December, has given to Yale University $10,000 for the establishment of the Ernest Howe Memorial Fund. The income of the fund will be used to promote the study of the geological sciences at Yale. Mr. Howe, who graduated from Yale College in 1898, was editor of the *American Journal of Science* from 1926 until his death. In addition to his research work, he was geologist of the Isthmian Canal Commission, was invited by the Mexican Government to reorganize its geological survey and was geologist on the scientific expedition to Brazil headed by Dr. Hamilton Rice under the auspices of the Royal Geographic Society of London. He was elected to a term in the Connecticut Legislature in 1920 and in 1924 was elected to the Connecticut Senate.

THE *Journal* of the American Medical Association reports that the one hundredth anniversary of the publication of William Beaumont's "Experiments and Observations on the Gastric Juice and the Physiology of Digestion" was celebrated by the St. Louis Medical

Society on November 21, the one hundred and forty-eighth birthday of Dr. Beaumont. The program was as follows: Dr. Major G. Seelig, "Biographical Sketch of William Beaumont"; Dr. Joseph Erlanger, "William Beaumont's Experiments and Their Present-Day Value"; Dr. Robert E. Schlueter, "Dr. Beaumont as a St. Louisan," and Dr. Louis H. Behrens, "Our Civic and Medical Debt to Beaumont." Photostatic copies of Dr. Beaumont's letters and documents, with other historical objects connected with his life and work, are on exhibition in the society's headquarters. Dr. Beaumont was president of the St. Louis Medical Society in 1840.

THE *British Medical Journal* reports that it is proposed to establish a lectureship in the University of Edinburgh, to be called the Sharpey-Schafer Lectureship in Physiology, to commemorate Professor Sir Edward Sharpey-Schafer, who has occupied the chair of physiology for thirty-four years and who has just retired. It is suggested that under this lectureship one lecture shall be given annually in Edinburgh by a distinguished physiologist to be suggested by the Faculty of Medicine. For this purpose a capital sum of about £1,000 is required, and an appeal has been issued for subscriptions to this fund, limited to a maximum of five guineas. Any persons desiring to contribute to the fund should send their subscriptions to the Dean of the Faculty of Medicine, University of Edinburgh.

RECENT DEATHS

DR. ROSCOE WILFRED THATCHER, research professor of chemistry at the Massachusetts State College, president of the college from 1927 to 1932, died suddenly while at work in the college laboratory on December 6. Dr. Thatcher was sixty-one years old.

DR. ALFRED FABIAN HESS, New York City, known for his work on rickets and other diseases of children, died suddenly on December 5, at the age of fifty-eight years.

OLOF AUGUST PETERSON, curator of mammalian paleontology at the Carnegie Museum, Pittsburgh, has died at the age of sixty-eight years.

THE sudden death at the age of eighty-one years is announced of George H. Barton, assistant professor of geology at the Massachusetts Institute of Technology from 1896 to 1904 and since 1902 director of the Teachers School of Science, conducted under the auspices of the extension department of Harvard University.

WHEATON BRADISH KUNHARDT, chairman of the board of directors and formerly president of the Carpenter Steel Company of Reading, Pennsylvania, manufacturers of tool, alloy and stainless steel, died suddenly on November 23, at the age of seventy-four years.

TILLMAN D. LYNCH, formerly consulting metallurgical engineer in charge of manufacturing and metallurgical processes at the Westinghouse Electric and Manufacturing Company, has died at the age of sixty-six years.

WILLIAM SHEAR, horticultural inspector at San Diego, California, died on November 6. He was born in Albany County, New York, December 31, 1868, graduated from the University of Nebraska, was a potato specialist for a number of years in the U. S. Department of Agriculture, and, later, with the State Department of Agriculture of California.

JOHN JOLY, professor of geology and mineralogy in the University of Dublin since 1897, died on December 8, at the age of seventy-six years.

THE death is announced of Dr. Jan B. Novak, general secretary of the Czech Academy of Science, on October 29. He was sixty-one years old.

THE death is announced of Dr. Albert Wangerin, professor of mathematics at Halle.

SCIENTIFIC EVENTS

APPOINTMENTS IN THE BUREAU OF PLANT INDUSTRY

THE appointment of Frederick D. Richey, now in charge of corn investigations in the Bureau of Plant Industry, as associate chief of that bureau, effective on January 1, has been announced by Secretary of Agriculture Henry A. Wallace. Mr. Richey will aid the chief of the bureau, Knowles A. Ryerson, whose appointment was recently announced, in the general administration of the department's largest scientific bureau, and will give special attention to research activities.

Mr. Richey succeeds Dr. Karl F. Kellerman, who will become head of a new Division of Plant Disease Eradication and Control in the Bureau of Entomology. This division will have transferred to it all activities directed toward the control and eradication of the phony peach disease, blister rust, barberry, citrus canker and Dutch elm disease.

Frederick D. Richey was born on September 3, 1884, in St. Louis, Mo. He received the degree of bachelor of science in agriculture from the University of Missouri in 1909 and immediately following his graduation managed a farm in northern Illinois. For one year, 1910–11, he was the food and drug commissioner of the State of Missouri. He has been with

the United States Department of Agriculture since 1911, engaged in corn investigations, and has been in charge of research work in this field since 1922. In this position he has made the corn investigational program entirely cooperative with the state experiment stations and has earned a reputation for ability in organizing effective cooperative research. He is the author of numerous publications and papers on corn growing, corn breeding and statistical methods.

In his new position, Dr. Kellerman will be able to devote his full time to plant disease work, a field in which he has been an outstanding leader for 20 years. Among numerous other activities, he organized in 1915, and has since directed, the cooperative campaign of the Gulf States and the Bureau of Plant Industry to eradicate citrus canker, one of the most contagious of all known diseases of citrus trees; his success in the citrus canker campaign is universally recognized as one of the most notable achievements ever recorded in disease eradication work.

Karl Frederic Kellerman was born of American parents in Göttingen, December 9, 1879. He received the degree of bachelor of science from Cornell University in 1900 and doctor of science from Kansas State College in 1923. He was an assistant professor in botany, Cornell University, 1900–1901; assistant physiologist, Bureau of Plant Industry, U. S. Department of Agriculture, 1901–1904; physiologist in charge of laboratory plant physiology, 1905–1906; physiologist in charge of soil bacteriology and water purification investigations, 1906–1914; assistant chief of the Bureau of Plant Industry, 1914–1917, and associate chief of bureau since 1917. Dr. Kellerman organized the *Journal of Agricultural Research* in 1913 and was chairman of the editorial committee from 1913–1924. In 1917 he was designated by President Wilson as a member of the National Research Council, serving as secretary of the agricultural committee, and since 1918 as a member of the division of biology and agriculture and of the division of federal relations.

SEMI-CENTENNIAL MEETING OF THE AMERICAN ORNITHOLOGISTS' UNION

THE Semi-Centennial Meeting of the American Ornithologists' Union, held in the American Museum of Natural History, New York City, from November 13 to 16, was the largest in the history of the union. Representatives were present from twenty-one states, the District of Columbia and three Provinces of Canada. Headquarters were at the Hotel New Yorker, where the business sessions were held. The public sessions were held in the museum. In connection with this meeting the union issued a memorial volume entitled "Fifty Years Progress of American Ornithology." An exhibit of "Birds in Art," numbering more than 300 entries, was installed in the education hall of the museum.

Officers for 1934 were elected as follows: *President,* J. H. Fleming; *Vice-presidents,* A. C. Bent, Taunton, Mass., and Herbert Friedmann, Washington, D. C.; *Secretary,* T. S. Palmer, Washington, D. C.; *Treasurer,* W. L. McAtee, Washington, D. C.; *Additional Members of the Council,* A. A. Allen, J. P. Chapin, Ruthven Deane, H. C. Oberholser, J. L. Peters, T. S. Roberts and P. A. Taverner.

The election of fellows and members included 1 fellow, John T. Zimmer, of New York; 3 corresponding fellows; 9 members, and 167 associates. The new corresponding fellows were Dr. J. M. Derscheid, Brussels, Belgium; Dr. Franz Groebbels, Hamburg, Eggendorf, Germany, and Dr. Pontus Palmgren, Helsingfors, Finland. The new members elected were M. A. Carriker, Beachwood, N. J.; S. T. Danforth, Mayaguez, P. R.; R. M. de Schauensee, Philadelphia, Pa.; J. O. Greenway, Jr., Cambridge, Mass.; J. M. Linsdale, Berkeley, Calif.; A. H. Miller, Berkeley, Calif.; J. D. Soper, Alberta, Canada; C. A. Urner, Elizabeth, N. J., and Francis M. Weston, Pensacola, Fla.

The Brewster Medal for the most meritorious work on American birds published during the last six years was awarded to Dr. Frank Michler Chapman for his "Birds of Eastern North America," 1932.

On Friday and Saturday trips were made to various points of interest, including Jones Beach Bird Sanctuary, Oyster Bay and Montauk, L. I.; the New York Zoological Park, and Barnegat Bay, N. J. More than 100 species of birds were observed at Jones Beach, Montauk and Barnegat Bay.

The next meeting will be held at the Field Museum in Chicago in October, 1934.

T. S. PALMER,
Secretary

SEMI-CENTENNIAL OF THE AMERICAN SOCIETY OF NATURALISTS

IN the month of March, 1883, Professor Samuel F. Clarke, of Williams College, issued a call for an association of American naturalists principally for the discussion of practical methods of technique and education, modified by the following addendum:

> It is further believed that such a society could materially influence for the better the cause of science in America; that it would have a very healthful general effect, and could exert a strong influence in many directions where at present it seems to be very much needed.

Of the fourteen naturalists who had expressed to Professor Clarke an interest in this enterprise, at least eleven appeared at the organization meeting in the Springfield High School Hall, Friday, April 10, in the year 1883, namely: Samuel F. Clarke, of Williams College; Alpheus Hyatt, of the Boston Society

of Natural History and the Massachusetts Institute of Technology; William T. Sedgwick, of the Massachusetts Institute; Charles S. Minot, of the Harvard Medical School; A. S. Packard, Jr., of Providence; William N. Rice, of Wesleyan University; J. M. Tylor, of Amherst; J. H. Pillsbury, of Springfield; H. N. Martin, of the Johns Hopkins University; Henry F. Osborn, of Princeton, and William B. Scott, of Princeton.

At first embracing geology and paleontology, as well as botany, zoology and physiology, the Society of Naturalists gradually drifted away from its original purposes, became an annual congress chiefly for the presentation and discussion of the most recent phases of zoological and biological research, but of late years has had as its objective "the association of working naturalists or biologists for discussing and correlating the broader problems of organic evolution with particular emphasis upon border-line fields of fundamental biology." The meetings are sometimes independent, but more often coordinated with those of many other biological associations of cognate purpose.

Of the original membership there appear to be only seven survivors, all of whom have been elected honorary members of the society, namely: Henry H. Donaldson, of Philadelphia; Simon H. Gage, of Ithaca; Samuel Henshaw, of Cambridge; C. Hart Merriam, of Washington; Henry Fairfield Osborn, of New York; William B. Scott, of Princeton, and Edmund B. Wilson, of New York.

A semi-centennial program has been arranged for the approaching Boston meeting. It will be presented on Saturday afternoon and evening, December 30. At the afternoon session the American Society of Naturalists will be joined by the American Society of Zoologists, the Botanical Society of America and the Genetics Society of America, and the session will be held in the auditorium of the New Lecture Hall, Harvard University. A symposium on "Biology and Society" will be presented, at which Dr. S. H. Gage, of Cornell University, who is one of the surviving original members of the American Society of Naturalists, will preside as honorary chairman. The symposium speakers will be Professor W. M. Wheeler, of Harvard University; Dr. E. A. Hooton, of Harvard University, and Dr. F. H. Hankins, of Smith College. Their respective topics will be: "Animal Societies," "Primitive Human Societies" and "Development of Modern Social Organizations." On Saturday evening the annual dinner of the American Society of Naturalists will be held in the Statler Hotel, which is designated as headquarters for the society. Following the dinner, Dr. E. G. Conklin, of Princeton University, will give an anniversary address on "Fifty Years of the American Society of Naturalists." This will be followed by the retiring presidential address, given by Dr. Burton E. Livingston, of the Johns Hopkins University, who will speak on "Environments."

Members of the American Society of Naturalists are specially invited to attend the William Thompson Sedgwick Memorial Lecture, presented under the auspices of the Massachusetts Institute of Technology and the American Association for the Advancement of Science, at 5 o'clock on Friday afternoon, December 29, this date being appropriately the seventy-eighth anniversary of the birthday of Professor Sedgwick. This memorial lecture will be given in the large Lecture Hall, Massachusetts Institute of Technology. The lecturer will be Professor Henry Fairfield Osborn, whose subject will be "Aristogenesis, the Creative Principle in the Origin of Species." Professor Osborn's address will be a sequel to one given by him at the ninth meeting of the American Society of Naturalists, held in 1890, also in Boston, on a topic of paramount interest at that time, namely, "Are Acquired Variations Inherited?" That earlier address may be read in the *American Naturalist*, for March, 1891.

THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

THE Local Committee for the Boston meeting wishes to call the attention of members of the association to some of the arrangements that have been made for the entertainment of visiting members, and especially to events that are scheduled for Wednesday, December 27. It is hoped that the great majority of those coming to Boston may plan their arrival so that they may be registered at Memorial Hall, Cambridge, or at the Massachusetts Institute of Technology, in time to participate in affairs which have been arranged for the afternoon.

Special attention is drawn to a concert by the Boston Symphony Orchestra. The Local Committee takes great pleasure in announcing that it has been able to arrange for a special Symphony Concert, in honor of the visiting members of the American Association for the Advancement of Science. This has been made possible through the cooperation of Dr. Serge Koussevitzky, the conductor, and the directors of the Boston Symphony Orchestra. This concert will be held at Symphony Hall, corner of Massachusetts Avenue and Huntington Avenue, on Wednesday afternoon, December 27, from 4 to 5 o'clock. Doors close promptly at 4:00. Admission is only by special ticket, which can be obtained at registration headquarters of the association at Memorial Hall, Cambridge, or at the subsidiary registration desk in the

main lobby of the Massachusetts Institute of Technology. The reputation of the Boston Symphony Orchestra guarantees a concert of the highest quality, and the local committee hopes that a large audience will be present.

Two other events of Wednesday afternoon are offered for the entertainment of visitors. Both of these are scheduled for the 2 to 3 hour in order that they may not conflict with the concert. Dr. H. E. Ives will give an illustrated lecture on "Scientific Simplification of the Artists' Palette," at the New Lecture Hall, Harvard University (across the street from Memorial Hall).

At Huntington Hall, Rogers Building, 491 Boylston Street, Boston, Dr. Charles H. Tozier will present a "Demonstration of the Value of Color Photography in Teaching All Branches of Natural Science." This demonstration will be a showing of lantern slides prepared by the use of color photography. The subjects chosen for illustration include minerals, rock-sections, geological formations, corals, birds, fish, and other zoological material, trees, flowers, etc. Of special interest will be slides made from histological sections of both normal and pathological tissues as seen under high magnification, even by the use of the oil immersion lens.

It is believed that this is the first public showing of these slides demonstrating histological structures and staining reactions, in which the colors are reproduced with extreme fidelity and accuracy. This demonstration will be of exceptional interest to teachers of the natural sciences and to research workers in microscopic anatomy.

The Rogers Building houses the Department of Architecture of the Massachusetts Institute of Technology. It is adjacent to the Boston Society of Natural History, the collections of which may easily be visited before or after this demonstration.

The scientific exhibits arranged in connection with this meeting of the association are in Memorial Hall, Cambridge, and will be open for inspection from Wednesday morning throughout the week.

Members of the association attending the meetings in Boston will find supplementary transportation service from the various Boston hotels to the Massachusetts Institute of Technology and Harvard University as follows:

From Hotels Bradford, Statler, Brunswick, Westminster, Copley-Plaza and Lenox, special bus service will be provided. Trips will be run from the Bradford, at 8:30, 8:45, 9:00, 9:15, 1:00, 1:15 and 1:30. These buses will stop at the Statler near the corner of Arlington Street and St. James Avenue three minutes later, in front of the Public Library, Copley Square, six minutes later than the above times. They are scheduled to arrive at the Massachusetts Institute of Technology twenty minutes after the starting time and at Harvard (Memorial Hall) twenty-seven minutes after the starting time.

Return service will be provided from Memorial Hall at 3:15 only on Wednesday for Massachusetts Institute of Technology, Symphony Hall, Public Library, Hotel Statler and Hotel Bradford. On Thursday, Friday and Saturday buses will leave Memorial Hall at 12:15, 12:30, 12:45, 4:45, 5:00, 5:15 for Massachusetts Institute of Technology, Public Library, Hotel Statler and Hotel Bradford. The leaving times from Massachusetts Institute of Technology will be seven minutes later for each trip.

A fare of ten cents for transportation in either direction will be collected when leaving the buses at Massachusetts Institute of Technology or Harvard University on the outbound trips and when boarding the buses on the inbound trips.

Members staying at the Buckminster or Kenmore Hotels can board an inbound subway car at Kenmore Station and change at Massachusetts Station, going upstairs for a surface car marked "Harvard" and alight at Massachusetts Institute of Technology or Harvard Square, as desired. Members registering at the Parker House or the Bellevue can most conveniently take Cambridge-bound subway trains at Park Street. The Massachusetts Institute of Technology is about seven minutes' walk from Kendall Station. The Harvard Square subway station is about three minutes' walk from Memorial Hall.

S. C. PRESCOTT,
Chairman, Local Committee

SCIENTIFIC NOTES AND NEWS

THE Medal of the Southern Medical Association for notable achievements in research was awarded to Dr. Wm. de B. MacNider, Kenan research professor of pharmacology in the University of North Carolina, at the recent annual meeting of the association held at Richmond, Virginia.

THE Royal Meteorological Society has awarded the Symons Gold Medal for 1934 to Sir Gilbert T. Walker. The medal is awarded biennially for distinguished work in connection with meteorological science and will be presented at the annual general meeting of the society on January 17.

THE Buckston Browne Prize Essay of the Harveian Society of London has been awarded to Dr. Lionel S. Penrose, for his essay on "The Influence of Heredity in Disease."

FREDERICK JOHN MARRIAN STRATTON, professor of astrophysics in the University of Cambridge, has been elected a corresponding member of the Instituto de Coimbra, Portugal.

THE title of emeritus professor has been granted to the following, who have recently retired from the staff of the University of Leeds: Professor A. F. Barker (textile industries); Professor J. F. Dobson (surgery); Professor W. Garstang (zoology); Professor J. Strong (education), and Professor R. A. Veale (therapeutics, pharmacy and materia medica).

THE British Institution of Civil Engineers has recently awarded a Telford Gold Medal and the Indian Premium to Mr. Robert Mair, Calcutta, and a George Stephenson Gold Medal and a Webb Prize to H. W. H. Richards, London. The awards are made for papers read and discussed at ordinary meetings.

DR. CHARLES H. MAYO, Rochester, Minnesota, was made president-elect of the Interstate Post-Graduate Medical Association of North America at the recent annual meeting in Cleveland. Dr. John M. T. Finney, Baltimore, became president.

DR. CHARLES H. KEENE, professor of hygiene at the University of Buffalo, has been elected vice-president of the American Association of School Physicians.

THE following officers of the University of Durham Philosophical Society have been elected for the year 1933–34: *President,* Professor R. A. Sampson; *Honorary General Secretary,* W. M. Madgin; *Honorary Treasurer,* J. W. Bullerwell; *Editor,* Professor G. W. Todd; *Assistant Editor,* J. F. Wood; *Honorary Librarian,* Dr. F. Bradshaw; *Assistant Librarian,* E. Patterson.

DR. GEORGE H. PARKER, professor of zoology at Harvard University, has leave of absence for the academic year 1934–35. Dr. William J. Crozier, professor of general physiology, and Dr. Kirk Bryan, associate professor of physiography, have leave of absence for the first half of the year.

THE reorganization of the Division of Organic Chemistry at the University of Minnesota has been completed by the promotion of Professor L. I. Smith to chief of the division to succeed the late Professor William H. Hunter. Professor Walter M. Lauer resumed his duties after spending a year in the laboratories of Professor Wieland in Munich and of the late Professor Prégl in Graz. Drs. P. D. Bartlett and C. F. Koelsch have been added to the staff. A new and enlarged organic research laboratory has been equipped and put into operation. Courses in microchemical and qualitative and quantitative analysis of organic compounds have been initiated.

THE governing body of the British Post-Graduate Medical School has appointed dean of the school Dr. M. H. MacKeith, fellow of Magdalen College and dean of the Medical School of the University of Oxford. The foundation stone of the new school, which will adjoin and be associated with the London County Council Hospital, Hammersmith, was laid by the chancellor of the exchequer on July 17. It is hoped that the school will be open to students towards the end of 1934.

THE following appointments have recently been made at the University of Sheffield: W. J. Lytle, to be lecturer in surgery; W. J. Mitchell, to be junior research assistant in glass technology, and H. Laithwaite to be research fellow in glass technology.

H. G. FORDER, head of the mathematical department of Hymers College, Hull, has been appointed professor of mathematics at Auckland University, New Zealand.

AT a meeting of the trustees of the British Museum on November 22 the Right Hon. Lord Macmillan was elected to the board of trustees, in the place of the late Viscount Grey of Fallodon.

THE British Secretary of State for the Colonies has recently made the following Colonial agricultural appointments: E. J. Gregory to be manager of the St. Augustine Experimental Station, Trinidad, and A. Thompson, assistant mycologist, to be mycologist of the Agricultural Department, Malaya.

A. G. HOVEY has left the research staff of the General Electric Company to become director of research of Beck, Koller and Company, Inc., Detroit, Mich.

ROSWELL MILLER, JR., of the American Museum of Natural History, has made zoological studies of the coral reefs of Tahiti and has photographed in color on motion picture film the coral reef life of the sea floor. He was accompanied by Harry L. Shapiro, who continued investigations in physical anthropology among the natives of the island.

PROFESSOR EDWARD KASNER, of Columbia University, addressed the American Mathematical Association on "Polygons and Groups" at a meeting at New Brunswick on December 2.

DR. HARLAN T. STETSON, director of the Perkins Observatory of the Ohio Wesleyan University, delivered a lecture on "Cosmic-Terrestrial Relations" before the Amateur Astronomical Society, at the American Museum of Natural History in New York on November 15.

PROFESSOR MAX BERGMANN, director of the Kaiser Wilhelm Institute in Dresden, gave a lecture entitled "Some Recent Work in the Chemistry of Proteins

and Amino Acids" at the George Washington University School of Medicine on November 28.

DR. RICHARD S. UHRBROCK, head of the research department in the Industrial Relations Division of the Procter and Gamble Company, addressed the University of Cincinnati Chapter of Sigma Xi on "The Scope of Industrial Psychology" on December 5.

THE one hundredth anniversary of the birth of Alfred Nobel, founder of the Nobel awards, will be celebrated throughout the world on Monday, December 18, and the Committee of One Hundred formed in this country will be the host to the American Nobel prize laureates at a dinner to be given in the evening at the Hotel Roosevelt, New York City. Dr. George J. Ryan, president of the New York City Board of Education, will be the chairman of the dinner, and Professor John Dewey, chairman of the Reception Committee of One Hundred, will act as toastmaster. The American Nobel laureates who have, so far, stated that they will be able to attend are Dr. Nicholas Murray Butler, Ambassador Frank B. Kellogg, Jane Addams, Sinclair Lewis, Dr. Irving Langmuir and Dr. R. A. Millikan. Professor Albert Einstein, who was awarded the prize in physics in 1921, will be a special guest of honor. The event is sponsored by the World Peaceways, under the auspices of a group of civic and social organizations, and the Committee of One Hundred is composed of distinguished leaders in social, economic, business and political circles. Headquarters for the Nobel Centennial Committee have been established at the Hotel Roosevelt. Nobel laureates will be the speakers. They will discuss national and international issues.

A SERIES of lectures in London was recently given on various aspects of the Houston Mount Everest Flight Expedition and an exhibition of photographs and instruments and other equipment relating to the expedition was opened on November 29. The lecturers were: Colonel P. T. Etherton on "The Human Element in the Expedition"; E. C. Shepherd on "The News Side"; L. V. Stewart Blacker on "The Technical and Photographic Side," and Olaf Bloch on "The Infra-Red Process."

THE third Grassland Conference of the North and Central European countries will be held from July 18 to 28, 1934, at Zurich, Switzerland, under the chairmanship of Dr. A. Volkart, president of the Federal Polytechnical School in Zurich. Information in regard to the conference can be had from the Federal Experimental Station for Agriculture, Zurich-Oerlikon, Switzerland. Besides the regular meetings of the conference, there will be various visits to alpine experiment stations, farms and pastures so that the visitor will have an opportunity to study alpine agriculture.

THE London *Times* writes editorially on November 8: "The International Conference for the Protection of the Fauna and Flora of Africa has just brought a useful week's work to a successful close. Representatives of all the African governments, with the one exception of Liberia, and of all the governments with possessions in Africa have agreed upon the terms of a convention which, when it is ratified and made operative, should check the progressive extinction of the varied species of wild life, animal and vegetable, once so abundant in the continent. In it provision is made both for the establishment of national parks and other reserves, in which the killing or capture of game and the collection or destruction of plants shall be limited or entirely prohibited, and for the control of hunting outside these reserved areas as well as of the traffic in trophies. The convention was signed yesterday by the delegates of the governments of Great Britain, France, Spain, Italy, Belgium, Portugal, South Africa, Egypt and the Sudan. It was further agreed that the work now set in hand should be continued by further conferences held at appropriate intervals to examine the practical effect of the convention and to consider any improvements which may suggest themselves. The government of Great Britain was requested to call together the next conference within four years."

THE faculty of Arts and Sciences of Harvard University voted on December 5 that in place of the Division of Philosophy there be created a Division of Philosophy and Psychology, and that in place of the department of philosophy and psychology there be created two departments, the department of philosophy and the department of psychology.

A RESOLUTION confirming the amalgamation of the Ross Institute with the London School of Hygiene and Tropical Medicine was passed unanimously at a meeting of the members of the Ross Institute on November 27. The resolution also confirmed the arrangement with the Seamen's Hospital Society, under which the hospital at the Ross Institute will be closed down and the patients received into the Tropical Hospital of the Seamen's Hospital Society.

CONGREGATION at the University of Oxford has made a grant of £100 to the expedition which is to leave at the end of this term for Ellesmere Land, in the Arctic, to the north of Baffin Bay. The expedition is being organized by Ernest Shackleton, of Magdalen College, son of the famous explorer and president of the Oxford Exploration Club, and will consist of members of the club.

A HERBARIUM of approximately 50,000 specimens

and a portion of their extensive botanical library have been presented to the University of Michigan by Parke, Davis and Company, of Detroit. This adds to the herbarium a collection of approximately 15,000 Michigan plants made by Dr. O. A. Farwell during the past thirty years. It is also rich in early collections of historic and taxonomic importance. Among others are specimens of Buckley, Chapman, Mohr, Bigelow, Shuttleworth, Heller, Rusby, Curtis, Nash, Lemmon and Sukdorf from the United States; of Rusby, Bang, Morong and Triana from South America; of Pringle, Palmer, Orcutt, Tuerckheim and Schaffner from Mexico and Central America; of Teysmann, De Vriese, Korthals, Duthie, Hooker, Wallich, Meissner and Mez from the East Indies and British India; of von Mueller, Maiden and Morrison from Australia; of Heller from Hawaii; of Boissier, Schimper, Schweinfurth, Schlechter and Burchell from the Levant and Africa.

THE late Alexander Legge, first chairman of the Federal Farm Board, left $900,000 to found an organization "devoted to the general welfare of the farming population of the United States and improvement of the conditions of rural life." Mr. Legge was president of the International Harvester Company.

ACCORDING to *Museum News*, the Public Works Administration has allotted $16,500 for repairs to the major ruins in Mesa Verde National Park, Colorado, and $17,175 for repairs to the Aztec Ruins in Aztec Ruin National Monument in New Mexico. In the Mesa Verde, stabilization work is planned at Cliff Palace, Balcony House, Square Tower House, Far View House and Pipe Shrine House to check disintegration of walls, to secure the preservation of these buildings without further extensive repairs, and to contribute to the safety of visitors. The need for these repairs had become acute because of settling in the loose fill on which Cliff Palace is built and because of seepage getting at the base of the retaining walls at Balcony House. At the other ruins wall strengthening, drains and certain capping of rooms is needed. At Aztec Ruins the work will include restoration as well as protective measures for certain parts of the ruin, especially the great Kiva.

A NEW farm tillage laboratory, in which studies will be made to find the types of machines best suited economically to the soils of the Southeast, will be built by the U. S. Department of Agriculture, at the Alabama Polytechnic Institute, Auburn. The Federal Bureau of Agricultural Engineering will construct nine shallow pits, each 20 feet wide, 250 feet long and 2 feet deep. Into each pit will be dumped 10 carloads of topsoil, a sample of one of the agricultural soils of the Southeast, ranging from sand to tight clay. In these parallel pits practical comparative tests of plows and cultivating machinery will be made at one location, working under controlled conditions. R. B. Gray, chief of the mechanical equipment division of the bureau, will supervise the new laboratory work. John W. Randolph, a bureau engineer, will have charge of experiments and will work in cooperation with M. L. Nichols, head of the department of agricultural engineering at the Alabama Institute.

DISCUSSION

UNIVERSITY PATENTS

SINCE the publication of my communication on "University Patents" in the number of SCIENCE for March 10, 1933, I have learned that there were inaccuracies in the following sentences from that article which invalidate any inferences that the patent in question was being exploited as a source of revenue for profit or research, or that there was the intent to control the patent for any other purpose than ensuring the quality of the product controlled by the patent:

> Without the aid of newspaper files many medical scientists can recall a trial which is reported to have cost the defendants $80,000. Duly skeptical of such a figure, I should, however, assume that the patentees did not use all their takings that year for research. Shortly after the trial they were told by a spirited chief of one city health service that he was going to use their process anyhow and on a large scale, for which he proposed to pay them just one dollar, and if they wanted to refuse this offer and bring suit, maybe they'd win, but the city was right and had good lawyers.
>
> A well-known American patent for the treatment of an important infectious disease is protected in one country abroad by a clause which forbids its use in research directed to its improvement.

ALAN GREGG

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NOVEMBER 29, 1933

THE EXPANDING LITERATURE[1]

IT is perhaps not unnatural that as the universe expands under the watchful tutelage of Sir Arthur Eddington to a point where few persons other than he can comprehend its vastness, the scientific literature about its contents should also expand to an extent such that most scientists are utterly unable to cope with more than a fraction of that covering any one branch of knowledge. We are inevitably driven to

[1] With apologies to the author of "The Expanding Universe."

read more and more about less and less. We are specialists.

But, even in our specialized narrow fields, the literature has expanded till one can keep pace with it, if at all, only by dint of considerable sacrifice of time that other people spend in some respite from the daily grind. This pressure of the literature is the direct result of a general expansion of research activities during the past fifteen years. It indicates in some measure the rapidity of the forward march of science, and is therefore to be welcomed. The deplorable thing is that the scientist must waste a certain portion of the all-too-short time available for reading in covering a literature unnecessarily cluttered up with inconclusive progress reports and with material re-hashed under two or three different titles and published with variously modified trimmings in as many different journals.

The first line of defense against the rising tide of literature is established by the abstracting journals. Though they provide no substitutes for the original papers, they do guide the research worker to the literature in his field. The more quickly and efficiently they do so, the more is the time available for actual research and the less is the waste of effort from unnecessary duplication of research. The difficulties faced by the abstracting journals are obviously matters of concern to all who use them. The following discussion of some of those difficulties in a recent editorial in *Nutrition Abstracts and Reviews*[2] is so pertinent that it might well be brought to the attention of workers in all fields of science:

> In many cases essentially the same material is published in two or more journals. When the papers, including the titles, are identical, no confusion is caused. In many cases, however, the results of the same experiments are published under slightly different headings, and even published separately by the different authors who have collaborated in the research. This increases the already almost impossible task of readers who try to read the original papers on their subject. As far as this journal is concerned, it involves duplication of abstracting, which increases the work and cost of producing the journal, without adding to its value. It is suggested that duplicate publication is usually unnecessary, and should be avoided. In cases where it is considered justifiable to write up the same material twice, it should be made clear at the beginning of the article, or in a footnote to the title, that the results have already been communicated and the original reference should be given.
>
> Another cause contributing to the present enormous output of literature is premature publication of results. This frequently leads to the appearance of a series of papers while the work is still in progress, involving considerable repetition in the description of procedure and the statement of partial findings. This custom is of no lasting advantage to the worker, and from the point of view of the advancement of knowledge it is to be deprecated. The premature publication of undigested data and hastily reached conclusions, which require subsequent revision, results in the confusion rather than the clarification of knowledge. The reputation of workers and the convenience of readers would be better served if authors could be persuaded to defer publication until the work was reasonably complete and ample time had been given to the study of data. The Editors venture to suggest that senior workers, who they are confident share these opinions, should take the opportunity of impressing them upon those working under their supervision.

[2] Vol. III, No. 1, 1933.

Apart from relief for the abstracting journals, it is obvious that elimination of unnecessary publication would simplify the literature problem for the individual worker, for the libraries that aid him and for persons and departments attempting to compile card indices covering special fields. Equally important is the fact that any reduction in the flood of manuscripts now entering nearly every editorial office in the country would automatically shorten the periods of imprisonment for papers now waiting from six months to a year or more for their release.

The paragraphs quoted above happened to meet the writer's eye at a time when he had just finished reading the third of three papers presenting the same data under three different titles. The present outburst is the result. It is in no sense directed at the volume of research but solely at the unnecessary and expensive publication which makes a difficult task almost impossible. The editors of *Nutrition Abstracts and Reviews* render a valuable service in pointing out that relief from this undesirable situation lies in the hands of scientific workers themselves.

F. B. H.

THE NEED OF ADEQUATE PROVISION FOR THE QUANTITY PRODUCTION OF DEUTERIUM WATER

THE recent work of G. N. Lewis,[1] of Crist and Dalin,[2] of Bonhoeffer and Brown[3] and of Oliphant[4] has shown that metathetical reactions involving the two isotopes of hydrogen must be of very general occurrence. This of course means that the preparation of many chemical compounds containing deuterium substituted for all or part of the hydrogen atoms will be comparatively simple as soon as pure deuterium water is available in quantity. To transform an ordinary hydrogen compound into the corresponding deuterium compound, one has evidently only to bring the compound into metathetical equilibrium with successive portions of pure deuterium water. Its replace-

[1] *Jour. Am. Chem. Soc.*, 55: 3502, 1933.
[2] *Jour. Chem. Phys.*, 1: 677, 1933.
[3] *Z. physik. Chem.*, 23: 171, 1933.
[4] *Nature*, 132: 675, 1933.

able hydrogens will then all be exchanged for deuterium.

Different conditions with respect to temperature, time, presence of suitable surface catalysts, etc., will be needed in different cases, but the principle is evidently of very general application. An example would be the bubbling of NH_3 gas through a train of bubble-tubes containing deuterium water and with suitable provision for drying the gas between tubes. From the end of such a train, deuterammonia, $NH^2{}_3$, would be evolved.

Similarly, if benzoic acid be shaken with successive portions of pure deuterium water it will probably be quantitatively converted into the corresponding deuterium acid, probably benzodeuteric acid, $C_6H^1{}_5COOH^2$. To prepare deuterobenzoic acid, $C_6H^2{}_5COOH^2$, would probably require a higher temperature and a suitable catalyst. This acid, if shaken with successive portions of pure protium water, $(H^1{}_2O)$ would probably yield deuterobenzoprotic acid, $C_6H^2{}_5COOH^1$.

The comparative ease with which many new compounds can be prepared in this way gives further emphasis to the great need of provision for the large-scale production of heavy water. To equip a small plant having a capacity of 6 to 10 gallons of 95 per cent. deuterium water per year would cost something like $25,000. Labor costs would be about $5,000 per year, and power costs (40 KW) would depend upon location. Such a plant would be much more economical than the small-scale laboratory outfits now in use at a number of universities and would produce sufficient heavy water to allow many chemical and biological investigations to be carried out.

In contrast with the hundreds of millions which are being spent in new projects by the Federal Government and by private industry, the amount of money involved is almost infinitesimal. Yet probably in no other way could the expenditure of an equal amount of money be productive of greater advances in chemistry and possibly biology and medicine, not to mention physics, which requires only relatively small amounts of the heavy water.

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ALFALFA YELLOWS

FOLLOWING the publication of the abbreviated discussion on "alfalfa yellows" (SCIENCE, October 27, 1933) we have been informed by Professor E. M. Searls, of the Department of Economic Entomology of the University of Wisconsin, that he had secured data from the entomological view-point, which lead essentially to the same conclusions with reference to leafhopper populations and time of cutting alfalfa, as expressed by us. This lends much emphasis to the validity of the findings, and because Professor Searls has not yet published his results we take this opportunity to provide for a simultaneity of recognition for his contribution.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

A PORTABLE VACUUM TUBE VOLTMETER FOR MEASUREMENT OF GLASS ELECTRODE POTENTIALS WITH EXAMPLES OF pH ESTIMATIONS[1]

SIMPLICITY of design, small cost, accuracy and stability of the zero point are factors which justify a brief description of an equipment which has been found extremely useful in measuring the pH of biological fluids, food products and the like. Any laboratory possessing a suitable potentiometer and galvanometer may be provided with equipment for measurements with a glass electrode for a sum not exceeding ten dollars. The necessary parts are: One R. C. A. tube No. 232, thirteen flashlight cells, four No. 6 dry cells, two single-pole single-throw switches, twenty-five feet of rubber insulated wire No. 16 B. and S. gauge, and a wide mouth bottle, with tight-fitting rubber stopper.

The vacuum-tube is kept in a dry atmosphere by mounting in the wide mouth bottle in the following manner: An eighteen-inch length of insulated wire is soldered to each of the four base prongs, and a twelve-inch length to the cap of the tube. The wires attached to the prongs are bent so that when the tube is in a vertical position the five wires may be passed through small holes in the rubber stopper, in which they should fit snugly. A dry atmosphere is maintained either by a thin layer of phosphorus pentoxide in the bottom of the bottle, or by means of phosphorus pentoxide contained in a side arm connecting through the rubber stopper.

The wiring diagram is shown in Fig. 1. The tube filament is supplied with 1.5 volts, four No. 6 dry cells connected in parallel to give sufficient capacity for the maintenance of a constant filament temperature. Seven flashlight cells, connected in series to the filament battery, furnish twelve volts to the screen or space charge grid. Four flashlight cells in series furnish six volts to the plate, acting through a galvanometer which has a sensitivity of 0.025 microamperes

[1] Food Research Division Contribution No. 176.

per millimeter of scale deflection, a coil resistance of 1,000 ohms and a period of 3 seconds.

The negative terminal of the plate battery connects with the positive galvanometer terminal of the potentiometer and the negative side of the tube filament, and with a ground if necessary. The cap, or control grid, is given a -1.5 volt charge by a flashlight cell connected in series with the negative galvanometer terminal of the potentiometer. Single-pole single-throw switches are placed in the filament circuit and the potentiometer storage cell circuit for convenience of operation. The zero point of the galvanometer is adjusted by utilizing the torque of the galvanometer suspension to counterbalance the rotation of the coil produced by the plate current.

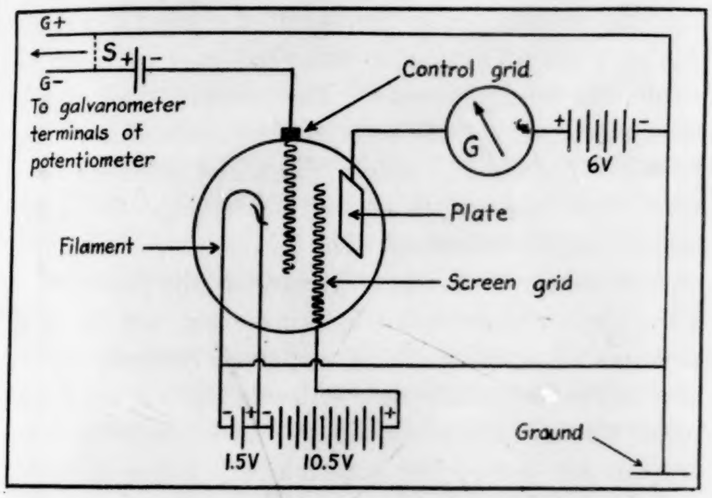

FIG. 1. Wiring diagram of vacuum-tube voltmeter, using R. C. A. 232 tube.

Differences in tube characteristics may occur among tubes of the same type, and therefore it may be necessary to alter slightly the voltages specified for the plate and space charge grid. This may be easily accomplished by keeping the charge applied to the cap or control grid constant at 1.5 volts $\pm$ 10 millivolts and varying the voltages in question until throwing the potentiometer out of balance 10 millivolts causes a deflection of the beam of light of at least four millimeters on the galvanometer scale.

By introducing a counter E.M.F. to control the zero point of the galvanometer, it becomes possible to alter the voltages applied to the plate and space charge grid so as to obtain a much greater sensitivity, but this complicates the circuit and offers no great practical advantage.

If a Leeds and Northrup type K potentiometer is used, the terminals marked G − and G + in Fig. 1 are joined to the galvanometer terminals of the potentiometer. Use of the student type potentiometer, or in fact any potentiometer not provided with a short circuiting key, necessitates the use of a short circuiting switch at S to connect G − and G + when the zero setting of the galvanometer is being adjusted.

Keeping the tube in a dry atmosphere eliminates erratic behavior due to electrical leakage over the tube and base. By using the galvanometer specified above with enclosed lamp and scale, a deflection of five millimeters is obtained when the potentiometer is thrown out of balance ten millivolts.

Several months' experience with this simple equipment has shown that the zero point is stable, even in the absence of shielding and ground connections. The elimination of elaborate shielding, the use of No. 6 dry cells and flashlight cells in place of storage cells, and the method of balancing the galvanometer in the plate circuit makes possible a simple piece of equipment which may be made portable by assembly in a small box.

The thickness of membranes in routine use ranges from 0.25 to 1.0 millimeter. However, as discussed in a previous publication,[2] precautions are taken to eliminate the "deviation film." The presence of this film not only requires the use of thin membranes but is a cause of erratic behavior. Several years of experience with the glass electrode has shown that a proper design of the electrode, making possible the elimination of the "deviation film," is more important than the use of extremely thin membranes and elaborate shielding of the measuring equipment.

The close agreement of a thick glass electrode and a hydrogen electrode was demonstrated by titrating a fifth molar disodium phosphate solution with 5 per cent. hydrochloric acid. The pH measured with the hydrogen electrode changed from 8.25 to 6.84, eleven measurements being made during the titration. The E.M.F. of the glass electrode measured against the hydrogen electrode remained constant at 303 ± 1 millivolts throughout the titration.

Recent studies[3] in this laboratory concerned with the toxic action of dinitrophenol, an agent which stimulates tissue metabolism, heat production and respiration, afforded an opportunity to observe the hydrogen-ion activity of the blood with the glass electrode. Two control measurements thirty-five minutes apart showed a pH of 7.30 for the arterial blood before injection of the dinitrophenol. Fifteen minutes after administration of the dinitrophenol the respiratory rate increased and the pH rose to 7.34, remaining constant for thirty minutes. Then a change toward acidity developed, as shown by pH values of 7.16, 7.04 and finally 6.94 for a sample of blood taken one minute after death.

These observations show the usefulness of the glass electrode and vacuum-tube voltmeter for demonstrating the constancy of the pH of arterial blood during

[2] H. Kahler and Floyd DeEds, *Jour. Am. Chem. Soc.*, 53: 2998, 1931.

[3] M. L. Tainter, J. H. Boyes and F. DeEds, *Arch. Internat. Pharm. et Therap.*, xlv: 234, 1933.

the control period, the shift toward the alkaline side during the period of over-ventilation, and the subsequent shift to acidity when the alkali reserve and the ventilation fail to compensate for the trend toward acidity caused by increased katabolism. The value of 6.94 for the pH of arterial dog blood removed as soon as possible after death is in close agreement with previously reported observations[4] in which thinner membranes and a much more elaborate measuring equipment were used.

This equipment, used in conjunction with sturdy glass electrodes, should extend the usefulness of the glass electrode, as for example in the determination of soil acidity, and the measurement of hydrogen-ion activity in such materials as canned meats, vegetables and fruits by direct insertion of the electrode without separation of the liquid and solid material.

FLOYD DEEDS

BUREAU OF CHEMISTRY AND SOILS
U. S. DEPARTMENT OF AGRICULTURE
AND
STANFORD UNIVERSITY SCHOOL OF MEDICINE

[4] Carl Voegtlin, Floyd DeEds and H. Kahler, Public Health Reports, 45: 2223, 1930.

SPECIAL ARTICLES

ISOLATION OF A CRYSTALLINE PROTEIN FROM PANCREAS AND ITS CONVERSION INTO A NEW CRYSTALLINE PROTEOLYTIC ENZYME BY TRYPSIN

KÜHNE and Heidenhain showed that the proteolytic enzymes of the pancreas are completely inactive in fresh pancreas or in freshly secreted pancreatic juice.[1] The enzymes become active when mixed with the enterokinase of the small intestine, as found by Schepowalnikow, or when the pancreas is allowed to stand in slightly acid solution. According to Vernon, activation may also be brought about by small amounts of active trypsin. The mechanism of this activation has been the subject of controversy for many years.

This note describes the isolation from fresh pancreas of an active crystalline protein which is converted by minute amounts of trypsin into a powerful proteolytic enzyme. This enzyme has also been obtained in crystalline form. The inactive protein has been called chymo-trypsinogen and the active protein chymo-trypsin.

Pancreas was removed from cattle immediately after slaughter and immersed in M/8 cold sulfuric acid. The pancreas was then minced and extracted for 24 hours at 5° C. with two volumes M/8 sulfuric acid. This extract has no measurable proteolytic activity but becomes highly active upon the addition of enterokinase or upon the addition of relatively large amounts of active trypsin. The addition of relatively small amounts of active trypsin does not cause activation. The extract contains a protein which is soluble in 0.4 saturated ammonium sulfate but insoluble in 0.7 saturated ammonium sulfate. This protein may be crystallized from 0.25 saturated ammonium sulfate by the addition of saturated ammonium sulfate and adjustment of the pH to about 5.0. It crystallizes in the form of elongated prisms. About 1 gm of crystalline material may be prepared from one beef pancreas. The protein prepared in this way can not be activated by enterokinase but becomes powerfully active upon the addition of a very small amount of crystalline trypsin[2] or of any crude trypsin solution. The crude extract and the mother liquor from the crystals, on the other hand, are completely activated by kinase but not by small amounts of trypsin. This apparent contradiction is due to the fact that crude extracts contain some material which inhibits trypsin so that small amounts of trypsin are completely inactivated. When kinase is added to such crude extracts sufficient active trypsin is formed to overcome the inhibiting effect and this active trypsin changes the chymo-trypsinogen to chymo-trypsin.

CONVERSION OF CHYMO-TRYPSINOGEN TO CHYMO-TRYPSIN

Three grams of crystalline chymo-trypsinogen were dissolved in 400 ml. M/30 pH 7.6 phosphate buffer, 1 mg of crystalline trypsin added and the solution kept at 5° C. The activity increased rapidly and after 24 hours had reached a constant value of about 1,000 times that of the trypsin added. The time rate of increase in activity is logarithmic and not auto-catalytic. This indicates that the chymo-trypsinogen can not be activated by chymo-trypsin and control experiments confirm this conclusion. No measurable hydrolysis of the chymo-trypsinogen occurred during activation. The active protein was precipitated from this solution by bringing to 0.7 saturated ammonium sulfate. The filter cake was dissolved in twice its weight of M/100 sulfuric acid, ammonium sulfate added to slight turbidity, and the pH adjusted to about 4.0 with sodium hydroxide. The solution was allowed to stand at 22°

[1] For review of the literature see Carl Oppenheimer, "Die Fermente und Ihre Wirkungen," G. Thieme, Leipzig, fifth edition, Vol. II, p. 917.

[2] John H. Northrop and M. Kunitz, SCIENCE, 73: 262, 1931; *Jour. Gen. Physiol.*, 16: 267, 1932.

C. over night and about 2 gm of a crystalline protein in the form of plates appeared. The activity of this preparation is about one third that of the previously described crystalline trypsin with respect to the digestion of hemoglobin or casein. It is much less active than trypsin in liquefaction of gelatin but much more active in clotting milk. It does not clot blood and contains no amylase or lipase activity. The digestion of casein is carried much further than by the crystalline trypsin. The enzyme is evidently quite distinct from the trypsin previously isolated and may represent the "pancreatic rennet" of Vernon.

The chymo-trypsinogen has been recrystallized ten times and shows constant optical activity and constant proteolytic activity after activation by trypsin. Some samples showed a very slight proteolytic activity without activation which was equivalent to about 1/5000 of that of the activated material. This trace of activity is variable and is probably due to the presence of a small amount of active material.

The chymo-trypsin has been recrystallized three times and all fractions show constant optical activity and constant proteolytic activity as measured by digestion of hemoglobin, casein or gelatin, or rennet action.

There is reason to believe, therefore, that these preparations represent pure proteins, and that the proteolytic activity is a property of the protein molecule.

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DEER AS CARRIERS OF ANAPLASMOSIS

The possibility that deer might serve as a reservoir for anaplasmosis has been considered for some time. Through the assistance of Mr. Ronald P. Harville, the Division of Fish and Game furnished two deer—one, a southern black-tailed buck, *Odocoileus columbianus scaphiotus;* the other, a Rocky Mountain mule deer, *Odocoileus hemionus hemionus* (Raf.). Both these animals were obtained in areas from which no anaplasmosis has been reported in cattle.

The southern black-tailed deer, number 1, was brought to the laboratory in a very weak condition. It was heavily infested with ticks, of which a large number were removed and identified as *Dermacentor occidentalis, Dermacentor parumapertus* and *Ixodes ricinus californicus.* After removal of the ticks, the animal speedily recovered, but a microscopic examination of this deer's blood made some time afterwards revealed a few bodies resembling *Anaplasma.* To prove the animal a carrier, 5 cubic centimeters of its blood were injected into calf 2642 on December 6, 1932. No symptoms, blood changes nor marginal bodies were observed in the calf. Later, it received blood containing *Anaplasma* from carrier cow 454, and promptly developed the disease, showing mild symptoms and blood changes. Deer 1, therefore, was not proved to be a carrier at this time.

Immediately after this deer was bled for the injection of calf 2642 on December 6, it received 10 cubic centimeters of blood from cow 265, which later succumbed to anaplasmosis. Deer 1 never developed any symptoms or blood changes characteristic of the disease.

On March 22, 1933, 13 cubic centimeters of blood were taken from this deer and injected into bull 133. This animal exhibited none of the symptoms or blood changes observed in anaplasmosis. Later, it was infected with blood from carrier cow 2603 and developed a mild case.

On July 1, 1933, 20 cubic centimeters of blood were taken from deer 1 and inoculated into cow 842. This cow presented symptoms and blood changes typical of anaplasmosis and eventually recovered.

In the blood of the mule deer, number 2, no *Anaplasma* were observed; consequently, it was assumed that this animal was not a carrier. On April 15, 1933, 20 cubic centimeters of blood were injected into this deer from cow 2607, which died of the disease shortly afterwards. As a control, cow 2603 received 10 cubic centimeters of blood from 2607 at the same time. On May 3, 1933, numerous marginal bodies were observed in the blood of control cow 2603. The infection ran a severe course, but the cow recovered. Deer 2 never developed symptoms of anaplasmosis, and, of several blood examinations, no marginal bodies were noted except in one instance and they were too few to be regarded as other than suspicious.

To determine whether deer 2 would transmit the infection, blood was taken from it on May 24, 1933, and injected into cow 2615. This cow exhibited a typical blood picture; numerous marginal bodies were observed, the red corpuscle count dropped from 6,160,000 to 1,440,000 and other changes, such as anisocytosis and punctate basophilia, were noted. The symptoms were characteristic: constipation, rapid pulse and respiration, and progressive weakness, terminating in death on June 28, 1933. The autopsy showed the usual lesions: icterus in the subcutaneous tissue and peritoneum; pale, viscous blood; petechial hemorrhages on the epicardium; markedly enlarged and jam-like spleen; slightly icteric liver; a gall bladder distended with thick, dark-green bile; and mucus-covered fecal pellets in the colon. From all these findings, therefore, the diagnosis of anaplasmosis is conclusive.

On July 1, 1933, another cow, 501, received 20 cubic centimeters of blood from deer 2. As the infection progressed in this cow, an abundance of marginal bodies were noted in the blood; a severe anemia developed, no signs of regeneration appeared and the animal died on August 8, 1933. The pathological changes revealed at autopsy were characteristic of anaplasmosis, as in the case of the previous transmission.

From these experiments, it is evident that certain species of deer, at least, are carriers of anaplasmosis without presenting any symptoms or other definite signs of the disease themselves. By injecting cattle with blood from the southern black-tailed deer following its infection, one of two attempts to transmit the disease was successful. The animal which failed to become infected, 133, proved susceptible to infection later, although it developed only a mild type, suggesting that a certain small degree of resistance may have been conferred upon it by the injection of deer blood. In the case of the mule deer, both transmissions were successful, terminating in fatal cases of anaplasmosis.

Since these experiments prove that certain deer may be carriers and since deer in the wild state harbor a variety of ticks, some of which have been found to be vectors[1] of *Anaplasma,* the obvious conclusion is that deer may be a potential source of anaplasmosis.

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INHIBITION OF SELENIUM INJURY TO WHEAT PLANTS BY SULFUR

WHEAT plants grown in soil to which selenium in the form of sodium selenate is added at the rate of 15 p.p.m., or even less under some conditions, become characteristically chlorotic. The young leaf blades are often almost snow white, with green tips and midveins. A suggestion by Dr. J. E. McMurtrey that the chlorosis might be a symptom of sulfur deficiency (inferable from the view that absorbed selenium replaces sulfur in organic compounds of the plants[1]), and that decreasing the available sulfur might therefore accentuate the injury, led to the discovery of a striking effect of sulfur on the toxicity of selenium to wheat.

In both sand and solution cultures the toxicity of a given amount of sodium selenate varied according to the relative amount of sulfate in the nutrient solution. Where there was no sulfate present the plants died in the early seedling stage; where its concentration was high compared with that of the selenate the plants developed normally without visible injury. It was obvious that the death of the plants in the no-sulfur cultures and the injury of those with moderate amounts of sulfur were due to the presence of selenium rather than to a deficiency of sulfur, for the only effect of sulfur deficiency, as shown by the controls without selenium, was a paler green color. Evidently, these controls had received some extraneous sulfur, possibly from fumigants used in the greenhouse, or from impurities in the chemicals, which were of c. p. grade but not specially purified. The pH values of the nutrient solutions were not correlated with their toxicity.

Plants grown in water cultures with various selenium concentrations up to 28 p.p.m., the highest tried, were uninjured where the proportion of selenium to sulfur was 1:12 or less. Some of the leaves were chlorotic wherever the ratio was as high as 1:8, the injury being progressively more pronounced as the ratio increased. Where it was as high as 1:2 growth was largely inhibited. It is not assumed that these ratios are constant for wheat under all conditions although they have shown a surprising reproducibility under the conditions of these experiments.

Elemental sulfur as well as ammonium sulfate completely inhibited visible injury to wheat plants in soils to which sodium selenate was added. This inhibition of symptoms suggests that the entrance of selenium into plants and the consequent toxicity of such plants for animals[2] may be conditioned by the amount of available sulfur in the soil.

A paper presenting the evidence for the foregoing statements is being submitted to the *Journal of Agricultural Research.*

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